HHS Public Access

Author manuscript

Urol Oncol. Author manuscript; available in PMC 2019 June 01.

Published in final edited form as:

Urol Oncol. 2018 June ; 36(6): 308.e19–308.e25. doi:10.1016/j.urolonc.2018.03.008.

Sociodemographic disparities in chemotherapy treatment and impact on survival among patients with metastatic bladder cancer

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Abstract

Objective—To evaluate how socioeconomic status and other demographic factors are associated with the receipt of chemotherapy and subsequent survival in patients diagnosed with metastatic bladder cancer.

Methods—Using data from the California Cancer Registry, we identified 3,667 patients diagnosed with metastatic urothelial carcinoma of the urinary bladder between 1988 and 2014. The characteristics of patients who did and did not receive chemotherapy as part of the first course of treatment were compared using chi-square tests. Logistic regression was used to identify predictors of chemotherapy treatment. Fine and Gray competing-risks regression and Cox proportional hazards regression were used to estimate bladder cancer-specific and all-cause mortality, respectively.

Results—Less than half (46.3%) of patients received chemotherapy. Patients from the lowest socioeconomic quintile were half as likely to have chemotherapy as those from highest quintile (OR = 0.5, 95% CI: 0.4, 0.7). Unmarried patients were significantly less likely to receive treatment (OR = 0.6, 95% CI: 0.5, 0.7). Not receiving chemotherapy was associated with greater mortality from bladder cancer (sHR = 1.4, 95% CI: 1.3, 1.5) and from all causes (HR = 2.0, 95% CI: 1.8, 2.1).

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Conclusions—We found clear disparities in chemotherapy treatment and survival with respect to socioeconomic and marital status. Future studies should explore the possible reasons why patients with low socioeconomic status and who are unmarried are less likely to have chemotherapy.

Keywords

urinary bladder neoplasms; chemotherapy; neoplasm metastasis; drug therapy; cancer; epidemiology

1. INTRODUCTION

Bladder cancer represents an important public health problem, accounting for about 5% of all new cancer cases in the U.S. [1] In 2018, it is estimated there will be 81,190 new cases and 17,240 deaths due to bladder cancer [1]. This burden is expected to increase with an aging population [2]. About 5% of cases are metastatic at the time of diagnosis, and approximately 15–40% of high grade superficial tumors progress to advanced disease [3,4]. These patients have high mortality rates, with only about 5% of metastatic cancer patients surviving at least five years post-diagnosis [5]. Despite advances in treatment, there has been little improvement in survival for patients with metastatic bladder cancer over the last two decades [6].

This lack of improvement could be attributed to under-treatment for some patients. Chemotherapy is currently the standard first-line treatment for metastatic bladder cancer and has been shown to be effective in improving symptoms, slowing cancer growth, and prolonging survival [7,8]. Yet, despite the apparent efficacy, many patients with metastatic disease do not receive chemotherapy [6,9]. Such treatment disparities in patients with bladder cancer may contribute to differential survival across age [10], racial and ethnic groups [11,12], and between men and women [13]. However, few studies have specifically looked at the contribution of socioeconomic status (SES) to receipt of standard treatment for bladder cancer and survival. Better understanding of disparities in treatment and survival should lead to interventions to reduce these disparities.

In this large population-based study of patients with metastatic bladder cancer, we aimed (1) to evaluate how SES and other demographic factors (age, sex, race, and marital status) are associated with the receipt of chemotherapy, and (2) to assess how these factors affect survival from bladder cancer.

2. METHODS

Patients were identified through the California Cancer Registry (CCR), the single largest population-based state cancer registry in the U.S. [14] The CCR contains demographic, diagnostic, treatment, and outcome information on all reportable cancers diagnosed in California residents since January 1988. Persons included in this study were diagnosed with pathologically confirmed urothelial cell carcinoma of the urinary bladder in California between 1988 and 2014. All included cases were diagnosed with metastatic disease and

were at least 20 years old at time of diagnosis. Only first primary tumor cases were included, and patients diagnosed at autopsy or by death certificate only were excluded from analysis.

Neighborhood SES (nSES) was based on U.S. Census data on neighborhood characteristics of the patient address at the time of diagnosis, including educational attainment, occupation type, employment rate, median household income, poverty level, median rent, and house values. For cases diagnosed 1988–2005, nSES was computed using census-block group data from the Census 2000 Summary File. For patients diagnosed 2006–2014, nSES was determined from the 2007–2011 American Community Survey. These two data sources were combined to form quintiles at the block group level across the state [15,16]. Race/ethnicity was classified into four mutually exclusive groups: non-Hispanic white, non-Hispanic black, Hispanic, and Asian/Pacific Islander. Age at diagnosis was categorized into 20–64 years, 65–74 years, and 75 years and older. Marital status was dichotomized into married or single/unmarried (single/never married, divorced, or widowed). Patients were categorized as having received chemotherapy as part of their first course of treatment or not. The CCR defines first course treatment as all treatment received before disease progression or treatment failure.

Patient information was summarized, and the characteristics of patients who did and did not receive chemotherapy were compared using chi-square tests. Logistic regression was used to predict the receipt of chemotherapy. Odds ratios and their corresponding 95% confidence intervals were generated for crude models and a model adjusted for age, sex, race/ethnicity, nSES, marital status, and year of diagnosis. Fine and Gray competing-risks regression and Cox proportional hazard regression were used to estimate bladder cancer-specific and all-cause mortality, respectively. Both crude and adjusted hazard ratios and their corresponding 95% confidence intervals were calculated. Subdistribution hazard ratios (sHRs) were calculated for bladder cancer-specific mortality [17]. Follow-up time for mortality was calculated as the number of days between the date of diagnosis and date of death through the end of the follow-up period (December 31, 2014). Censoring was accounted for patients who were alive at the follow-up date or were lost to follow-up. Statistical significance was set at 0.05 for all analysis. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

3. RESULTS

A total of 3,667 patients with metastatic bladder cancer were identified. Patient characteristics are displayed in Table 1. A total of 1,427 (38.9%) patients were 75 years or older at the time of diagnosis, and most patients were male (68.7%), non-Hispanic white (75.5%), and married (52.8%). There were similar numbers of patients across nSES quintiles. The majority of patients (56.8%) were diagnosed between 2002 and 2014. Fewer than half (46.3%) of patients received chemotherapy as part of their first course of treatment.

Table 2 compares the characteristics of patients who received and did not receive chemotherapy. Receiving chemotherapy was associated with being 20–64 years old ($p<0.0001$), male ($p<0.0001$), and married ($p<0.0001$). Non-Hispanic black race was associated with not receiving chemotherapy ($p=0.0293$). There was an inverse relationship

with respect to treatment status and nSES (p for trend <0.0001). The proportion of patients receiving chemotherapy increased over time (p for trend <0.0001).

The results of the analysis of chemotherapy predictors are shown in Table 3. Adjusting for all other factors, patients aged 65–74 and 75 years and older were significantly less likely to receive chemotherapy than those aged 20–64 years (p<0.0001 for both). Females were significantly less likely to receive chemotherapy in crude analysis, but there was no significant association after adjustment (p=0.3836). Similarly, non-Hispanic blacks were significantly less likely to have chemotherapy in an unadjusted model, but this was no longer statistically significant in the adjusted model (p=0.3016). In both crude and adjusted analysis, patients diagnosed 2009–2014 were significantly more likely to receive chemotherapy (adjusted OR = 1.6, 95% CI: 1.3, 2.0, p<0.0001), indicating an increase in chemotherapy treatment in recent years.

After adjustment, unmarried patients were significantly less likely to receive chemotherapy (OR = 0.6, 95% CI: 0.5, 0.7, p<0.0001). There was a gradient effect with respect to nSES and treatment—the lower the nSES, the less likely a patient was to undergo chemotherapy. Patients from the lowest SES neighborhoods were half as likely to have chemotherapy as those from the highest SES neighborhoods (OR = 0.5, 95% CI: 0.4, 0.7, p<0.0001). This effect was even stronger among unmarried patients. Single patients in the lowest nSES quintile were 70% less likely to receive chemotherapy compared to married patients in the highest nSES group (OR = 0.3, 95% CI: 0.2, 0.5, p<0.0001).

Bladder cancer-specific and all-cause mortality estimates are presented in Table 4. Not receiving chemotherapy was significantly associated with about 40% greater mortality from bladder cancer (sHR = 1.4, 95% CI: 1.3, 1.5, p<0.0001) and twice the risk of death from all causes (HR = 2.0, 95% CI: 1.8, 2.1, p<0.0001). Adjusting for other factors, unmarried patients had a less favorable overall prognosis than married patients (HR = 1.2, 95% CI: 1.1, 1.3, p<0.0001). Patients from lower nSES groups had higher all-cause mortality than those from the highest nSES quintile, though there was no consistent trend across groups. Only Hispanic ethnicity was associated with reduced risk of death from bladder cancer. There was no change in cancer-specific or overall mortality over time. Gender was not associated with mortality after adjusting for other factors.

4. DISCUSSION

We undertook a large population-based study of California patients diagnosed with metastatic bladder cancer and found notable disparities in chemotherapy treatment and survival. Patients from lower SES neighborhoods and who were unmarried were significantly less likely to receive chemotherapy as part of the first course of treatment. This signifies an important area in need of intervention, as chemotherapy has been shown to improve survival in metastatic bladder cancer patients [18]. Indeed, we observed that not receiving chemotherapy was associated with worse survival. Our findings add to the increasing amount of evidence that disparate treatment and lower quality of care for cancer patients are linked with disproportionate survival across groups [19–21].

There are several possible explanations for why patients with low nSES may not undergo chemotherapy. People with low SES may have limited access to health care or have poorer baseline health. In a large, multistate registry-based study of breast, prostate, and colorectal cancer patients, researchers found patients living in low SES neighborhoods were less likely to receive aggressive treatment [19]. They noted that those under the age of 65 living in low SES areas were more likely not to have health insurance, and patients over 65 living in low SES areas were more likely to have comorbidities [19]. Not having insurance substantially increases patient health care costs, which may prevent a patient from pursuing expensive treatments. The existence of comorbidities further complicates cancer treatment and may be a major reason why a patient is not offered or refuses chemotherapy.

Structural barriers, such as geographical distance to the treatment facility and access to transportation, may also influence a patient's treatment [22]. A larger study of nearly 17,000 bladder cancer patients using Surveillance, Epidemiology, and End-Results (SEER) data found wide regional variation in treatment, which may reflect availability of physicians and patient proximity to treatment centers [23]. The authors also suggested that many patients with bladder cancer who are older or live in certain geographic areas and are denied aggressive therapy would actually benefit from such treatment [23]. Similarly, consistent with our findings, another population-based study using SEER data of 154 patients with muscle-invasive bladder cancer reported that although racial and sex differences did not significantly contribute to treatment, receipt of cystectomy and chemotherapy varied by geographic region, suggesting a lack of consensus in the treatment of bladder cancer [24].

It is also possible that physicians' recommendations impact treatment outcomes. Doctors may be influenced by their perception of a patient's willingness to comply with treatment or by their personal preferences or biases [22]. This can result in disparate clinical recommendations for racial minorities or patients of lower SES. Patients themselves may refuse to undergo chemotherapy, even if recommended by their physicians. This can be due to distrust of their provider or a lack of understanding of their treatment options or health condition [22].

Although we found that patients with low nSES were less likely to have chemotherapy, nSES was not as strong of a predictor for death from bladder cancer as it was for overall mortality. Similar to our findings, a prospective study of 1,537 patients with bladder cancer from the West Midlands region in England determined that less affluent groups had worse all-cause survival, but that SES was not significantly associated with bladder cancer-specific mortality [25]. One possible explanation for this discrepancy is that there may be competing risks that affect overall but not cancer-specific survival. For example, smoking tobacco is the most important cause of bladder cancer [26], and persons of lower SES are more likely to be current or former smokers. Poorer patients may thus be more subject to cardiorespiratory disease and other smoking-related illnesses that increase overall mortality risk.

We determined that patients who were unmarried were not only less likely to receive chemotherapy, but to have worse survival. This idea is supported by other studies. A large study of bladder cancer patients from the SEER-Medicare database indicated that married men at all stages of bladder cancer have better survival than unmarried men, even

independent of SES [27]. A spouse may encourage seeking care and provide psychosocial support [11], and it is suggested that such social support leads to better survival [11,20]. However, social support is less common among low-income and marginalized groups [20], which reflects our finding that the association of low nSES with receipt of chemotherapy was even stronger among unmarried patients.

We did not find significant associations of sex or race with treatment or survival, unlike other studies that reported an increased risk of death from bladder cancer for female and non-Hispanic black patients [13,28]. These survival disparities can be partly explained by differential distributions of important clinical prognostic factors, including tumor grade, diagnostic stage, and histologic type. For example, women and black patients tend to be diagnosed at more advanced stages [13,23,29], and black patients are also more likely to be diagnosed with histologic types associated with poorer survival [30]. However, our study was restricted to patients of the same disease stage and histologic type, which may explain why we did not observe significant effects of sex or race.

There are several important limitations in this study. We were unable to adjust for comorbidity in our analysis, as this data was not collected by CCR during the study period of interest. People with bladder cancer often have significant comorbidities [31], and patients in poor health may be less likely to undergo treatment. However, while cisplatin-based chemotherapy is recommended for fit patients [32], other regimens may still be suitable for those deemed unfit for cisplatin [32,33]. Less than half of patients in this study received any form of chemotherapy. If comorbidity drives this lack of treatment, then our findings underscore the urgent need to improve care for patients unfit to receive standard chemotherapy treatment [33]. Chemotherapy may be underreported to cancer registries, and availability of registry treatment data has previously been found to vary by hospital and patient characteristics [34]. However, we were only missing chemotherapy information for 77 (2.1%) patients, and patients with missing treatment information did not differ significantly from those included in analysis. Among patients who did not receive chemotherapy, we did not differentiate between patients who were offered but refused chemotherapy and patients for whom chemotherapy was not recommended.

Despite these limitations, our study was unique in several ways. This large population-based sample includes all patients diagnosed with metastatic bladder cancer in a socioeconomically and ethnically diverse state. Because we restricted our analysis to patients with the same stage at diagnosis and histologic type, we could control for clinical factors that impact both treatment type and prognosis. This allowed us to better assess the specific associations of sociodemographic factors with treatment and subsequent survival.

5. CONCLUSION

In this large population-based analysis of cancer registry data, we found clear disparities in chemotherapy treatment and survival with respect to socioeconomic and marital status. Patients who did not receive chemotherapy were more likely to be from poor neighborhoods and unmarried, and these same factors were associated with worse survival. In a future study, comorbidity should be accounted for to more accurately assess whether

sociodemographic factors are independently associated with chemotherapy treatment, and the possible reasons for disparate treatment should be explored.

Acknowledgments

The collection of cancer incidence data used in this study was supported by the California Department of Public Health as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885; the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract HHSN261201000140C awarded to the Cancer Prevention Institute of California, contract HHSN261201000035C awarded to the University of Southern California, and contract HHSN261201000034C awarded to the Public Health Institute; and the Centers for Disease Control and Prevention's National Program of Cancer Registries, under agreement U58DP003862-01 awarded to the California Department of Public Health. The ideas and opinions expressed herein are those of the author(s) and endorsement by the State of California, Department of Public Health the National Cancer Institute, and the Centers for Disease Control and Prevention or their Contractors and Subcontractors is not intended nor should be inferred.

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Table 1

Characteristics of patients diagnosed with metastatic bladder cancer in California, 1988–2014 (*N*=3,667).

Variable	N	%
Total	3,667	100.0
Age at Diagnosis		
20–64 years	1,139	31.1
65–74 years	1,101	30.0
75+ years	1,427	38.9
Sex		
Male	2,519	68.7
Female	1,148	31.3
Race/Ethnicity		
Non-Hispanic White	2,769	75.5
Non-Hispanic Black	230	6.3
Hispanic	438	11.9
Asian/Pacific Islander	212	5.8
Other/Unknown	18	0.5
Neighborhood Socioeconomic Status		
Highest	688	18.8
Upper-Middle	755	20.6
Middle	783	21.4
Lower-Middle	699	19.1
Lowest	607	16.6
Unknown	135	3.7
Marital Status		
Married	1,935	52.8
Single/Divorced/Widowed	1,645	44.9
Unknown	87	2.4
Year of Diagnosis		
1988–1994	754	20.6
1995–2001	830	22.6
2002–2008	1,021	27.8
2009–2014	1,062	29.0
Received Chemotherapy		
Yes	1,697	46.3
No	1,893	51.6
Unknown	77	2.1

Table 2

Comparison of patients who did and did not have chemotherapy as part of the first course of treatment for metastatic bladder cancer in California, 1988–2014 (*N*=3,590[+]).

Variable	Received Chemotherapy				
	Yes (*N*=1,697)		No (*N*=1,893)		P-Value
	N	%	N	%	
Age at Diagnosis					
20–64 years	718	42.3	389	20.6	<0.0001*
65–79 years	552	32.5	870	46.0	<0.0001*
80+ years	427	25.2	634	33.5	<0.0001*
Sex					
Male	1,234	72.7	1,234	65.2	<0.0001*
Female	463	27.3	659	34.8	<0.0001*
Race/Ethnicity					
Non-Hispanic White	1,286	75.8	1,427	75.4	0.7818
Non-Hispanic Black	91	5.4	135	7.1	0.0293*
Hispanic	211	12.4	213	11.3	0.2734
Asian/Pacific Islander	101	6.0	109	5.8	0.8051
Other/Unknown	8	0.5	9	0.5	0.9860
Neighborhood Socioeconomic Status					
Highest	370	21.8	304	16.1	<0.0001*
Upper-Middle	360	21.2	377	19.9	0.3362
Middle	353	20.8	413	21.8	0.4583
Lower-Middle	301	17.7	386	20.4	0.0436*
Lowest	253	14.9	339	17.9	0.0156*
Unknown	60	3.5	74	3.9	0.5556
Marital Status					
Married	1010	59.5	879	46.4	<0.0001*
Single/Divorced/Widowed	655	38.6	962	50.8	<0.0001*

Variable	Received Chemotherapy				P-Value
	Yes (*N*=1,697)		No (*N*=1,893)		
	N	%	N	%	
Unknown	32	1.9	52	2.8	0.0883
Year of Diagnosis					
1988–1994	327	19.3	415	21.9	0.0500 *
1995–2001	333	19.6	467	24.7	0.0003 *
2002–2008	465	27.4	536	28.3	0.5423
2009–2014	572	33.7	475	25.1	<0.0001 *

+ Chemotherapy information was missing or unknown for *N*=77 patients

* Indicates statistical significance at 0.05 level

Table 3

Results of logistic regression analysis for predicting receipt of chemotherapy among patients diagnosed with metastatic bladder cancer in California, 1988–2014.

	Crude		Adjusted[+]	
	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Age at Diagnosis				
20–64 years	Ref	–	Ref	–
65–74 years	0.6 (0.5, 0.7)	<0.0001*	0.5 (0.4, 0.6)	<0.0001*
75+ years	0.2 (0.2, 0.3)	<0.0001*	0.2 (0.2, 0.3)	<0.0001*
Sex				
Male	Ref	–	Ref	–
Female	0.7 (0.6, 0.8)	<0.0001*	0.9 (0.8, 1.1)	0.3836
Race/Ethnicity				
Non-Hispanic White	Ref	–	Ref	–
Non-Hispanic Black	0.7 (0.6, 1.0)	0.0394*	0.8 (0.6, 1.2)	0.3016
Hispanic	1.1 (0.9, 1.3)	0.3651	1.2 (0.9, 1.5)	0.2172
Asian/Pacific Islander	1.0 (0.8, 1.4)	0.8462	1.0 (0.7, 1.4)	0.9244
Neighborhood Socioeconomic Status				
Highest	Ref	–	Ref	–
Upper-Middle	0.8 (0.6, 1.0)	0.0232*	0.8 (0.6, 0.9)	0.0143*
Middle	0.7 (0.6, 0.9)	0.0009*	0.7 (0.5, 0.9)	0.0011*
Lower-Middle	0.6 (0.5, 0.8)	<0.0001*	0.6 (0.5, 0.7)	<0.0001*
Lowest	0.6 (0.5, 0.8)	<0.0001*	0.5 (0.4, 0.7)	<0.0001*
Marital Status				
Married	Ref	–	Ref	–
Single/Divorced/Widowed	0.6 (0.5, 0.7)	<0.0001*	0.6 (0.5, 0.7)	<0.0001*
Year of Diagnosis				
1988–1994	Ref	–	Ref	–
1995–2001	0.9 (0.7, 1.1)	0.3323	0.9 (0.7, 1.1)	0.4104
2002–2008	1.1 (0.9, 1.3)	0.3231	1.1 (0.9, 1.4)	0.3655
2009–2014	1.5 (1.3, 1.8)	<0.0001*	1.6 (1.3, 2.0)	<0.0001*

Abbreviations: OR = Odds Ratio, CI = Confidence Interval, Ref = Reference Group

[+]Adjusted for age at diagnosis, sex, race/ethnicity, neighborhood socioeconomic status, marital status, and year of diagnosis

*Indicates statistical significance at 0.05 level

Urol Oncol. Author manuscript; available in PMC 2019 June 01.

Table 4

Results of survival analysis for bladder cancer-specific and all-cause mortality of patients with metastatic bladder cancer in California, 1988–2014.

	Bladder Cancer Mortality				All-Cause Mortality			
	Crude		Adjusted+		Crude		Adjusted+	
	sHR (95% CI)	P-Value	sHR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value
Age at Diagnosis								
20–64 years	Ref	–	Ref	–	Ref	–	Ref	–
65–74 years	1.0 (0.9, 1.1)	0.7216	1.0 (0.9, 1.1)	0.5224	1.2 (1.1, 1.3)	0.0002*	1.1 (1.0, 1.2)	0.0236*
75+ years	1.1 (1.0, 1.2)	0.0066*	1.0 (0.9, 1.1)	0.7570	1.6 (1.5, 1.7)	<0.000 1*	1.3 (1.2, 1.4)	<0.000 1*
Sex								
Male	Ref	–	Ref	–	Ref	–	Ref	–
Female	1.1 (1.0, 1.2)	0.1209	1.0 (0.9, 1.1)	0.7558	1.1 (1.0, 1.2)	0.0320*	0.9 (0.9, 1.0)	0.0745
Race/Ethnicity								
Non-Hispanic White	Ref	–	Ref	–	Ref	–	Ref	–
Non-Hispanic Black	1.1 (0.9, 1.3)	0.3372	1.1 (0.9, 1.3)	0.4180	1.1 (1.0, 1.3)	0.1315	1.1 (0.9, 1.2)	0.3753
Hispanic	0.8 (0.7, 0.9)	0.0012*	0.8 (0.7, 1.0)	0.0074*	0.9 (0.9, 1.1)	0.3303	1.0 (0.9, 1.1)	0.5261
Asian/Pacific Islander	0.8 (0.7, 1.0)	0.0218*	0.9 (0.7, 1.0)	0.1008	0.9 (0.8, 1.1)	0.3246	1.0 (0.8, 1.1)	0.5373
Neighborhood Socioeconomic Status								
Highest	Ref	–	Ref	–	Ref	–	Ref	–
Upper-Middle	1.1 (0.9, 1.2)	0.3711	1.0 (0.9, 1.2)	0.6382	1.0 (0.9, 1.1)	0.6209	1.0 (0.9, 1.1)	0.8255
Middle	1.1 (1.0, 1.2)	0.0899	1.1 (1.0, 1.2)	0.1050	1.3 (1.1, 1.4)	<0.000 1*	1.3 (1.1, 1.4)	<0.000 1*
Lower-Middle	1.0 (0.9, 1.2)	0.5109	1.0 (0.9, 1.2)	0.7984	1.1 (1.0, 1.2)	0.0472*	1.1 (1.0, 1.2)	0.2125
Lowest	1.0 (0.9, 1.1)	0.6671	0.9 (0.8, 1.1)	0.3794	1.2 (1.1, 1.4)	0.0006*	1.2 (1.0, 1.3)	0.0178*
Marital Status								
Married	Ref	–	Ref	–	Ref	–	Ref	–
Single/Divorced/Widowed	1.1 (1.0, 1.2)	0.0099*	1.1 (1.0, 1.1)	0.1888	1.3 (1.2, 1.3)	<0.000 1*	1.2 (1.1, 1.3)	<0.000 1*
Year of Diagnosis								
1988–1994	Ref	–	Ref	–	Ref	–	Ref	–
1995–2001	1.0 (0.9, 1.1)	0.6101	1.0 (0.9, 1.1)	0.6459	1.0 (0.9, 1.1)	0.7321	1.0 (0.9, 1.1)	0.5718
2002–2008	0.9 (0.9, 1.0)	0.2784	1.0 (0.9, 1.1)	0.3981	1.0 (0.9, 1.1)	0.4524	1.0 (0.9, 1.1)	0.8507

	Bladder Cancer Mortality				All-Cause Mortality			
	Crude		Adjusted[+]		Crude		Adjusted[+]	
	sHR (95% CI)	P-Value	sHR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value
2009–2014	0.9 (0.8, 1.0)	0.0819	0.9 (0.8, 1.1)	0.3282	0.9 (0.8, 1.0)	0.0195*	0.9 (0.8, 1.0)	0.2461
Received Chemotherapy								
Yes	Ref	–	Ref	–	Ref	–	Ref	–
No	1.4 (1.3, 1.5)	<0.000 1*	1.4 (1.3, 1.5)	<0.000 1*	2.1 (2.0, 2.3)	<0.000 1*	2.0 (1.8, 2.1)	<0.000 1*

Abbreviations: sHR = Subdistribution Hazard Ratio, HR = Hazard Ratio, CI = Confidence Interval, Ref = Reference Group

[+]Adjusted for receipt of chemotherapy, age at diagnosis, sex, race/ethnicity, neighborhood socioeconomic status, marital status, and year of diagnosis

*Indicates statistical significance at 0.05 level